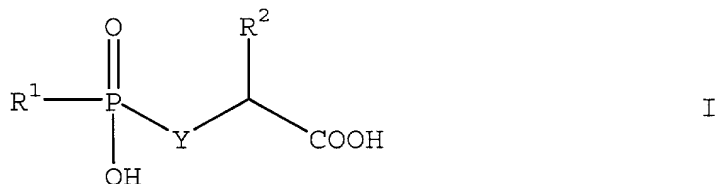


WE CLAIM:

1. A method for treating retinopathy, age-related macular degeneration or glaucoma comprising administering an effective amount of a NAALADase inhibitor to a mammal in need of such treatment.

2. The method of claim 1, wherein the NAALADase inhibitor is an acid containing a metal binding group.

3. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula I



or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

Y is CR^3R^4 , NR^5 or O;

R^1 is hydrogen, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_3 - C_8 cycloalkyl, C_5 - C_7 cycloalkenyl, Ar, COOR^6 , NR^6R^7 or OR^6 , wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s), preferably, independently selected from the group consisting of carboxy, C_3 - C_8 cycloalkyl, C_5 - C_7 cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C_1 -

C₆ alkyl, C₂-C₆ alkenyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, phenoxy, benzyloxy, COOR⁶, NR⁶R⁷ and Ar;

R² is hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, Ar, halo or carboxy, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s), preferably, independently selected from the group consisting of carboxy, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, phenoxy, benzyloxy, NR⁶R⁷ and Ar;

R³ and R⁴ are independently hydrogen or C₁-C₃ alkyl;

R⁵ is hydrogen or C₁-C₃ alkyl;

R⁶ and R⁷ are independently hydrogen, C₁-C₉ alkyl, C₂-C₉ alkenyl, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl or Ar, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s), preferably, independently selected from the group consisting of carboxy, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, phenoxy, benzyloxy and Ar; and

Ar is selected from the group consisting of 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 4-indolyl, 2-furyl, 3-furyl, tetrahydrofuranlyl, tetrahydropyranylyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl, wherein said Ar is unsubstituted or substituted with one or more substituent(s), preferably, independently

selected from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ alkoxy, C₂-C₆ alkenyloxy, phenoxy, benzyloxy, carboxy and N⁶R⁷.

5

4. The method of claim 3, wherein Y is CH₂.

5. The method of claim 4, wherein R² is -(CH₂)₂COOH.

10

6. The method of claim 5, wherein R¹ is hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, benzyl, phenyl or OR⁶, wherein said alkyl, alkenyl, cycloalkyl, cycloalkenyl, benzyl and phenyl are independently unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of carboxy, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ alkoxy, C₂-C₆ alkenyloxy, phenoxy, benzyloxy, NR⁶R⁷, benzyl and phenyl.

15

20

7. The method of claim 6, wherein the compound of formula I is selected from the group consisting of:

2-(phosphonomethyl)pentanedioic acid;

2-[[(2-carboxyethyl)hydroxyphosphinyl]methyl]-

25

pentanedioic acid;

2-[(benzylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[(phenylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[[[(hydroxy)phenylmethyl]hydroxyphosphinyl]-
methyl]pentanedioic acid;

2-[(butylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[[[(3-methylbenzyl)hydroxyphosphinyl]methyl]-
5 pentanedioic acid;

2-[(3-phenylpropylhydroxyphosphinyl)methyl]-
pentanedioic acid;

2-[[[(4-fluorophenyl)hydroxyphosphinyl]methyl]-
pentanedioic acid;

10 2-[(methylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[(phenylethylhydroxyphosphinyl)methyl]pentanedioic
acid;

2-[[[(4-methylbenzyl)hydroxyphosphinyl]methyl]-
pentanedioic acid;

15 2-[[[(4-fluorobenzyl)hydroxyphosphinyl]methyl]-
pentanedioic acid;

2-[[[(4-methoxybenzyl)hydroxyphosphinyl]methyl]-
pentanedioic acid;

2-[[[(3-trifluoromethylbenzyl)hydroxyphosphinyl]-
20 methyl]pentanedioic acid;

2-[[[4-trifluoromethylbenzyl)hydroxyphosphinyl]-
methyl]pentanedioic acid;

2-[[[(2-fluorobenzyl)hydroxyphosphinyl]methyl]-
pentanedioic acid;

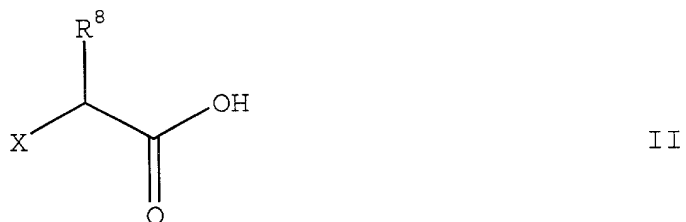
25 2-[[[(2,3,4,5,6-pentafluorobenzyl)hydroxy-
phosphinyl]methyl]pentanedioic acid; and

enantiomers and pharmaceutically acceptable
equivalents.

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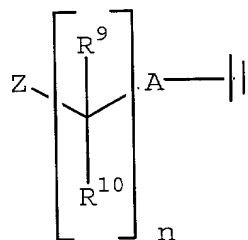
8. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula II

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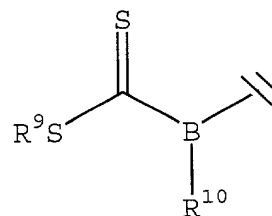


or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

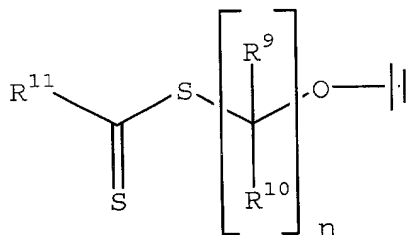
X is a moiety of formula III, IV or V



III



IV



V ;

5 R⁶, R⁹, R¹⁰, R¹¹, R¹², R¹⁴, R¹⁵ and R¹⁶ are independently hydrogen, C₁-C₉ alkyl, C₂-C₉ alkenyl, C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, Ar¹, hydroxy, carboxy, carbonyl, amino, cyano, isocyano, nitro, sulfonyl, sulfoxy, thio, thiocarbonyl, thiocyano, formanilido, thioformamido, 10 sulfhydryl, halo, haloalkyl, trifluoromethyl or oxy, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s); and

provided that when X is a moiety of formula III and A is O, then n is 2, 3 or 4; when X is a moiety of formula III and A is S, then n is 2, 3 or 4; and when X is a moiety of formula III and A is $(\text{CR}^{15}\text{R}^{16})_m\text{S}$, then n is 0, 2, 3 or 4.

9. The method of claim 8, wherein:
X is a moiety of formula III;
n is 0, 1, 2 or 3;
Z is SH, SO₃H, SO₂H, SOH or S(NHR¹²)₂R¹³; and
A is O, S or CR¹⁵R¹⁶.

10. The method of claim 9, wherein Z is SH.

11. The method of claim 10, wherein R^8 is $-(CH_2)_2COOH$.

5

12. The method of claim 10, wherein the compound of formula II is selected from the group consisting of:

2-(2-sulfanylethyl)pentanedioic acid;

3-(2-sulfanylethyl)-1,3,5-pentanetricarboxylic acid;

10 2-(2-sulfanylpropyl)pentanedioic acid;

2-(2-sulfanylbutyl)pentanedioic acid;

2-(2-sulfanyl-2-phenylethyl)pentanedioic acid;

2-(2-sulfanylhethyl)pentanedioic acid;

2-(2-sulfanyl-1-methylethyl)pentanedioic acid;

15 2-[1-(sulfanylmethyl)propyl]pentanedioic acid;

2-(3-sulfanylpentyl)pentanedioic acid;

2-(3-sulfanylpropyl)pentanedioic acid;

2-(3-sulfanyl-2-methylpropyl)pentanedioic acid;

2-(3-sulfanyl-2-phenylpropyl)pentanedioic acid;

20 2-(3-sulfanylbutyl)pentanedioic acid;

2-[3-sulfanyl-2-(phenylmethyl)propyl]pentanedioic acid;

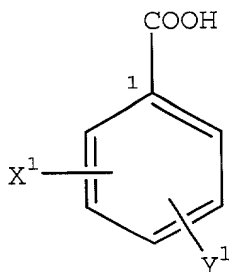
2-[2-(sulfanylmethyl)butyl]pentanedioic acid;

2-[2-(sulfanylmethyl)pentyl]pentanedioic acid;

25 2-(3-sulfanyl-4-methylpentyl)pentanedioic acid; and

enantiomers and pharmaceutically acceptable equivalents.

13. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula VI



VI

5 or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^1 is $-W-Z^1$;

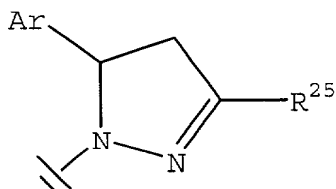
W is a bond or a linking group;

Z^1 is a terminal group; and

10 Y^1 is $-COOH$ oriented *meta* or *para* relative to C-1.

14. The method of claim 13, wherein:

X^1 is $-(CR^{17}R^{18})_nNH(CR^{19}R^{20})_mCOOH$, $-PO(OH)OR^{22}$,
 $-(CR^{17}R^{18})_nP(O)(OH)R^{22}$, $-NH-(CR^{19}R^{20})_m$ -heteroaryl,
 15 $-NH(P(O)(R^{23})OH)$, $-(CR^{17}R^{18})_nNH(P(O)(OH)R^{23})$, $-CON(R^{22})(OH)$
 $-(CR^{17}R^{18})_nCON(R^{22})(OH)$, $-(CR^{17}R^{18})_nSH$ or $-O(CR^{19}R^{20})_mSH$,
 $-SO_2NH$ -aryl, $-N(C=O)-CH_2(C=O)$ -aryl, $-SO_2NH$ -aryl,
 $-N(C=O)-CH_2(C=O)$ -aryl, $-O$ -aryl wherein aryl in $-O$ -aryl is
 20 substituted by at least one of nitro, carboxy or



wherein X^1 is oriented *meta* or *para* relative to C-1;

m and n are independently 1-3, provided that when X^1 is $-O(CR^{19}R^{20})_mSH$, then m is 2 or 3;

5 R^{17} , R^{18} , R^{19} , R^{20} , R^{22} , R^{23} and R^{25} are independently hydrogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino or C_1 - C_6 alkoxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle and alkoxy are independently unsubstituted or
10 substituted with one or more substituent(s); and

Y^1 is $-COOH$ oriented *meta* or *para* relative to C-1.

15 15. The method of claim 13, wherein the compound of formula VI is selected from the group consisting of

2-[(4-carboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

2-[(2,5-dicarboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

20 1,2,4-benzenetricarboxylic acid;

2-[(2-carboxyphenyl)thio]-1,4-benzenedicarboxylic acid;

2-bromo-1,4-benzenedicarboxylic acid;

2-amino-1,4-benzenedicarboxylic acid;

2-sulfoterephthalic acid, monosodium salt;

5 2-carboxymethyl-1,4-benzenedicarboxylic acid;

2-[(2-furanylmethyl)-amino]-1,4-benzenedicarboxylic
acid;

2-[(carboxymethyl) amino]-1,4-benzenedicarboxylic
acid;

10 4-(4-nitrobenzoyl)-1,3-benzenedicarboxylic acid;

4-[4-(2,4-dicarboxybenzoyl)phenoxy]-1,2-benzene-
dicarboxylic acid;

4-[[(2,4,6-trimethylphenyl) amino] carbonyl]-1,3-benzenedicarboxylic acid;

15 4-nitro-1,3-benzenedicarboxylic acid;

4-[(1-naphthalenylamino)-carbonyl]-1,3-benzene-
dicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

4-[(2-carboxyphenyl)thio]-1,3-benzenedicarboxylic
20 acid;

4-[3-[3-(2,4-dicarboxyphenoxy)propyl]dithio]-
propoxy]-1,3-benzenedicarboxylic acid;

4-hydroxy-1,3-benzenedicarboxylic acid;

4-[(2-furanylmethyl)amino]-1,3-benzenedicarboxylic
25 acid;

4-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid;

5-[4,5-dihydro-5-(4-hydroxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-1,3-benzenedicarboxylic acid;

5 5-(4,5-dihydro-3-methyl-5-phenyl-1H-pyrazol-1-yl)-1,3-benzenedicarboxylic acid;

5-[[[4-chloro-3-nitrophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

10 5-[[[4-chloro-3-[[3-(2-methoxyphenyl)-1,3-dioxopropyl]amino]phenyl]amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-[[3-[4-(acetylamino)phenyl]-1,3-dioxopropyl]amino]-1,3-benzenedicarboxylic acid;

5-acetylamino-1,3-benzenedicarboxylic acid;

15 5-[[[1-hydroxy-2-naphthalenyl)carbonyl]-methyldamino]-1,3-benzenedicarboxylic acid;

5-(4-carboxy-2-nitrophenoxy)-1,3-benzenedicarboxylic acid;

5-sulfo-1,3-benzenedicarboxylic acid;

5-nitro-1,3-benzenedicarboxylic acid;

20 5-amino-1,3-benzenedicarboxylic acid;

1,3,5-benzenetricarboxylic acid;

5-[[[3-amino-4-chlorophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5- (3-mercaptopropoxy) -1,3-benzenedicarboxylic acid;

5-hydroxy-1,3-benzenedicarboxylic acid;

5- (2-mercaptoethoxy) -1,3-benzenedicarboxylic acid;

5- [(hydroxyamino) carbonyl] -1,3-benzenedicarboxylic
5 acid;

5-phosphono-1,3-benzenedicarboxylic acid;

5-mercaptomethyl-1,3-benzenedicarboxylic acid;

5-phosphonomethyl-1,3-benzenedicarboxylic acid;

5- [[(carboxymethyl) amino] -methyl] -1,3-benzene-
10 dicarboxylic acid;

5- [(carboxymethyl) amino] -1,3-benzenedicarboxylic
acid;

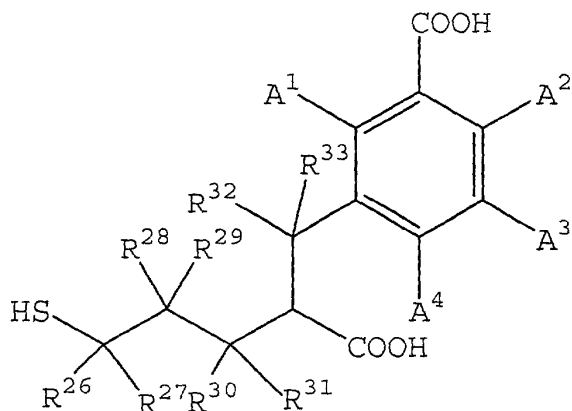
5- [[(2-furanylmethyl) amino] -methyl] -1,3-benzene-
dicarboxylic acid;

15 5- [2- (hydroxyamino) -2-oxoethyl] -1,3-benzene-
dicarboxylic acid;

5- (2-mercaptoethyl) -1,3-benzenedicarboxylic acid; and
enantiomers and pharmaceutically acceptable
equivalents.

20

16. The method of claim 1, wherein the NAALADase
inhibitor is a compound of formula VII



VII

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} and R^{33} are independently hydrogen or C_1 - C_3 alkyl;

A^1 , A^2 , A^3 and A^4 are independently hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo, nitro, phenyl, phenoxy, benzyl, benzyloxy or $-COOH$, or any adjacent two of A^2 , A^3 and A^4 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic ring, said heterocyclic aromatic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s).

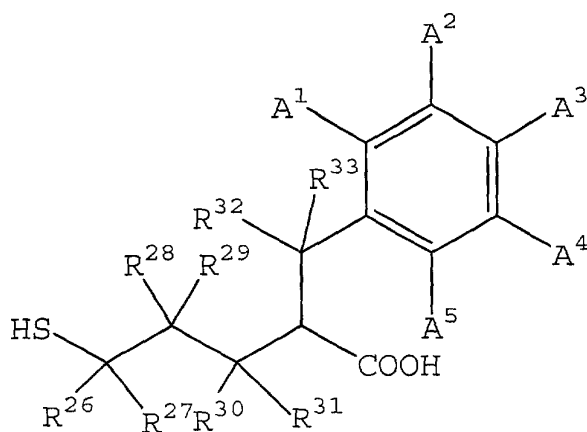
17. The method of claim 16, wherein:

R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} and R^{33} are independently hydrogen or methyl; and

A^1 , A^2 , A^3 and A^4 are independently hydrogen, C_1 - C_4 alkyl, C_1 - C_2 alkoxy, halo, nitro, phenyl, phenoxy, benzyloxy, nitro or $-COOH$.

18. The method of claim 16, wherein any adjacent two of A^2 , A^3 and A^4 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic ring, said heterocyclic aromatic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s).

19. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula VIII



VIII

10 or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} and R^{33} are independently hydrogen or C_1 - C_3 alkyl; and

15 A^1 , A^2 , A^3 , A^4 and A^5 are independently hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_3 perhaloalkyl, phenyl, phenoxy, benzyl, benzyloxy, hydroxy, halo, cyano, nitro, $-SO_2R^{34}$, $-(C=O)NR^{34}R^{35}$, $-(C=O)NR^{34}(CH_2)_nCOOH$, $-NR^{34}(C=O)R^{35}$, $-(CH_2)_nCOOH$ or $-COOH$, or any adjacent two of A^1 , A^2 , A^3 , A^4 and A^5 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic ring, said heterocyclic aromatic

20

R³⁴ and R³⁵ are independently hydrogen, C₁-C₆ alkyl, phenyl or benzyl; and

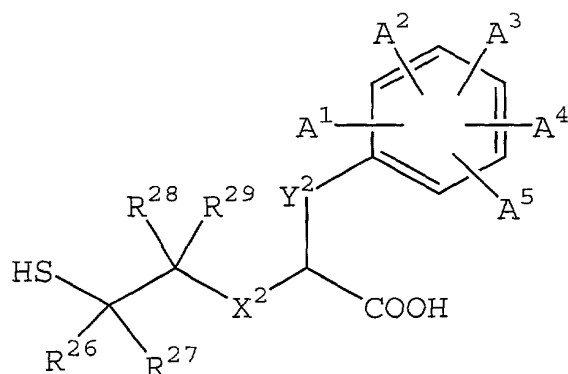
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20. The method of claim 19, wherein:

R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{32} and R^{33} are each hydrogen;

10

22. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula IX



IX

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

5 X^2 and Y^2 are independently $-CR^{30}R^{31}-$, $-O-$, $-S-$ or $-NR^{30}-$, provided that at least one of X^2 and Y^2 is/are $-CR^{30}R^{31}-$;

10 A^1 , A^2 , A^3 , A^4 and A^5 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, $-COOR^{34}$, $-COR^{34}$, $-NR^{34}R^{35}$, $-SR^{34}$, $-SOR^{34}$, $-SO_2R^{34}$, $-SO_2(OR^{34})$, $-(C=O)NR^{34}R^{35}$, $-(C=O)NR^{34}(CH_2)_nCOOH$, $-NR^{34}(C=O)R^{35}$ or $-(CH_2)_nCOOH$, or any adjacent two of A^1 , A^2 , A^3 , A^4 and A^5 form with the benzene ring a fused ring that is saturated or unsaturated, aromatic or non-aromatic, and carbocyclic or heterocyclic, said heterocyclic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s);

n is 1-3;

20 R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{31} , R^{34} and R^{35} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and said alkyl,

alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy, and fused ring are independently unsubstituted or substituted with one or more substituent(s).

5

23. The method of claim 22, wherein:

Y^2 is -O-, -S- or $-NR^{30}-$;

A^1 , A^2 , A^3 , A^4 and A^5 are independently hydrogen, C_1 - C_4 alkyl, C_1 - C_2 alkoxy, hydroxy, halo, -COOH, -COR³⁴,
10 -NR³⁴(C=O)R³⁵ or -(CH₂)COOH; and

R³⁴ and R³⁵ are independently hydrogen or methyl.

24. The method of claim 22, wherein:

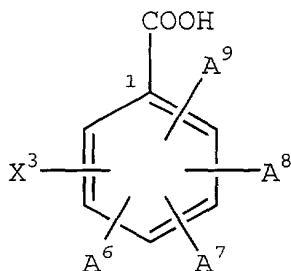
Y^2 is $-CR^{30}R^{31}-$;

15 A^1 , A^2 , A^3 and A^4 are each hydrogen; and

A^5 is phenoxy, benzyloxy, aryl, heteroaryl, carbocycle or heterocycle, wherein said phenoxy and benzyloxy are substituted with -COOH, and said aryl, heteroaryl, carbocycle and heterocycle are independently
20 substituted with one or more substituent(s) selected from the group consisting of cyano and -COOH.

25. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula X

"000000" 000000



X

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

5 X^3 is $-(CR^{36}R^{37})_nSH$, $-O(CR^{36}R^{37})_2SH$, $-S(CR^{36}R^{37})_2SH$ or $-NR(CR^{36}R^{37})_2SH$;

n is 1-3; and

10 R , R^{36} , R^{37} , A^6 , A^7 , A^8 and A^9 are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyno, isothiocyno, formamido, thioformamido, sulfo, sulfinio, C_1 - C_9 alkylsulfonyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenoxy, 15 phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s).

26. The method of claim 25, wherein the compound of formula X is selected from the group consisting of:

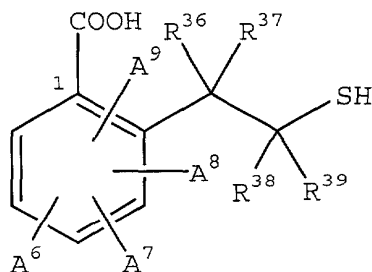
- 20 3-(2-mercaptoethyl)-benzoic acid;
3-(mercaptomethyl)-benzoic acid;
2-(mercaptomethyl)-benzoic acid;
5-hydroxy-2-(2-mercaptoethyl)-benzoic acid;

- 2-(2-mercaptoethyl)-benzoic acid;
- 5-[(4-carboxyphenyl)methoxy]-2-(2-mercaptoethyl)-benzoic acid;
- 2-(2-mercaptoethyl)-5-(phenylmethoxy)-benzoic acid;
- 5 2-(carboxymethoxy)-6-(2-mercaptoethyl)-benzoic acid;
- 5-[(3-carboxyphenyl)methoxy]-2-(2-mercaptoethyl)-benzoic acid;
- 2-(2-mercaptoethyl)-6-(phenylmethoxy)-benzoic acid;
- 2-[(2-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;
- 10 2-[(4-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;
- 3-(2-mercaptoethyl)-[1,1'-biphenyl]-2,3'-dicarboxylic acid;
- 15 2-(3,3-dimethylbutoxy)-6-(2-mercaptoethyl)-benzoic acid;
- 2-(2-mercaptoethyl)-6-(2-phenylethoxy)-benzoic acid;
- 2-[(2-chlorophenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;
- 20 2-[[3-carboxy-5-(1,1-dimethylethyl)phenyl]methoxy]-6-(2-mercaptoethyl)-benzoic acid;
- 2-(2-mercaptoethyl)-6-phenoxy-benzoic acid;
- 2-(2-mercaptoethyl)-6-phenylamino-benzoic acid;
- 2-(2-mercaptoethyl)-6-(phenylthio)-benzoic acid;
- 25 5'-(1,1-dimethylethyl)-3-(2-mercaptoethyl)-[1,1'-biphenyl]-2,3'-dicarboxylic acid;
- 3-(2-mercaptoethyl)-[1,1'-biphenyl]-2,4'-dicarboxylic acid;

4-(mercaptomethyl)-[1,1'-biphenyl]-2,3'-dicarboxylic
acid;

5-(mercaptomethyl)-2-(phenylmethoxy)-benzoic acid;
 and
 4-bromo-3-(mercaptomethyl)-benzoic acid; and
 enantiomers and pharmaceutically acceptable
 5 equivalents.

27. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XI



XI

10 or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

R^{37} , R^{38} , R^{39} and R^{40} are independently hydrogen or C_1 - C_3 alkyl;

15 A^6 , A^7 , A^8 and A^9 are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thioccyano, isothiocyano, formamido, thioformamido, sulfo, sulfinio, C_1 - C_9
 20 alkylsulfonyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenoxy, phenoxy and benzyloxy are independently unsubstituted or

substituted with one or more substituent(s).

28. The method of claim 27, wherein:

R^{36} , R^{37} , R^{38} and R^{39} , A^7 , A^8 and A^9 are each hydrogen;

5 A^6 is hydrogen, $-(CH_2)_n-W^1$, or $-Y^3-(CH_2)_n-W^1$;

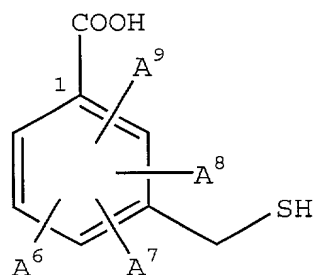
n is 0-3;

Y^3 is O, S or NR^{40} ;

R^{40} is hydrogen or C_1 - C_4 alkyl; and

10 W^1 is C_1 - C_6 alkyl or phenyl, wherein W^1 is unsubstituted or substituted with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, carboxy or halo.

29. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XII



XII

15

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

20 A^6 , A^7 , A^8 and A^9 are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfinio, C_1 - C_9 alkylsulfonyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenoxy, phenoxy or

benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenoxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s).

5

30. The method of claim 29, wherein:

A^7 , A^8 and A^9 are each hydrogen;

A^6 is $-(CH_2)_n-Ar^2$ or $-Y^3-(CH_2)_n-Ar^2$;

n is 0-3;

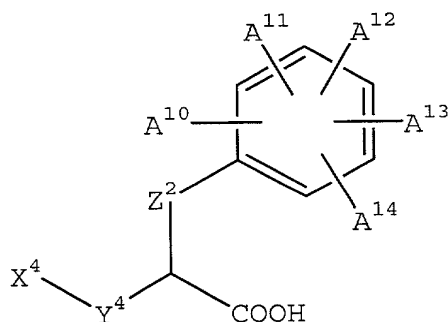
10 Y^3 is O, S or NR^{41} ;

R^{41} is hydrogen or C_1-C_4 alkyl; and

Ar^2 is phenyl, wherein Ar^2 is unsubstituted or substituted with C_1-C_4 alkyl, carboxy or halo.

15

31. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XIII



XIII

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

20

X^4 is $-(CO)NHOH$ or $-N(OH)COH$;

Y^4 is a bond or a divalent linking group having from

1 to 9 carbon atom(s) and from 0 to 5 heteroatom(s) independently selected from the group consisting of oxygen, sulfur and nitrogen;

Z^2 is $-CR^{41}R^{42}-$, $-NR^{41}-$, $-O-$ or $-S-$;

5 A^{10} , A^{11} , A^{12} , A^{13} and A^{14} are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, $-COOR^{43}$, $-COR^{43}$, $-NR^{43}R^{44}$, $-SR^{43}$, $-SOR^{43}$, $-SO_2R^{43}$, $-SO_2(OR^{43})$,
10 $-(CO)NR^{43}R^{43}$, $-(CO)NR^{43}(CH_2)_nCOOH$, $-NR^{43}(CO)R^{44}$ or $-(CH_2)_nCOOH$, or any adjacent two of A^{10} , A^{11} , A^{12} and A^{13} form with the benzene ring a fused ring that is saturated or unsaturated, aromatic or non-aromatic, and carbocyclic or heterocyclic, said heterocyclic ring containing 1 or 2
15 oxygen, nitrogen and/or sulfur heteroatom(s);

n is 1-3;

R^{41} , R^{42} , R^{43} and R^{44} are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and

20 said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy, and fused ring are independently unsubstituted or substituted with one or more substituent(s).

32. The method of claim 31, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, $-O-$, $-S-$ or $-SO_2-$;

p and q are independently 0-4; provided that when q is 0 and W^2 is $-NR^{49}-$, $-O-$, $-S-$ or $-SO_2-$, then Z^2 is $-CR^{41}R^{42}-$;

R^{45} , R^{46} , R^{47} , R^{48} , R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfinio, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s); and

A^{10} , A^{11} and A^{12} are each hydrogen.

33. The method of claim 32, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$;

p is 0-4;

q is 0;

R^{45} , R^{46} , R^{47} , R^{48} , R^{49} and R^{50} are each hydrogen;

A^{10} , A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen, $-COOR^{43}$, C_1-C_4 alkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl; and

A^{14} is $-COOR^{43}$.

34. The method of claim 32, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-S-$;

p and q are independently 1-4;

R^{45} , R^{46} , R^{47} , R^{48} , R^{49} and R^{50} are independently
5 hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl or
phenyl;

A^{10} , A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4
alkynyl, phenyl, benzyl, phenoxy, benzyloxy or halo,
10 wherein said alkyl, alkenyl, alkynyl, phenyl, benzyl,
phenoxy and benzyloxy are independently unsubstituted or
substituted with carboxy; and

A^{14} is $-COOH$.

15 35. The method of claim 32, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, $-O-$, $-S-$ or $-SO_2-$;

p and q are independently 0-4, provided that when q
is 0 and W^2 is $-NR^{49}-$, $-O-$, $-S-$ or $-SO_2-$, then Z^2 is
20 $-CR^{41}R^{42}-$;

R^{45} , R^{46} , R^{47} , R^{48} , R^{49} and R^{50} are independently
hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl,
heteroaryl, carbocycle, heterocycle, halo, hydroxy,
sulfhydryl, nitro, amino, cyano, isocyano, thiocyano,
25 isothiocyano, formamido, thioformamido, sulfo, sulfinio, C_1-
 C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein
said alkyl, alkenyl, alkynyl, aryl, heteroaryl,
carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and

benzyloxy are independently unsubstituted or substituted with one or more substituent(s);

A¹⁰, A¹¹ and A¹² are each hydrogen;

A¹³ is hydrogen; and

5 A¹⁴ is benzyl or carboxybenzyl.

36. The method of claim 31, wherein the compound of formula XIII is selected from the group consisting of:

3-*tert*-butyl-5-(2-carboxy-3-hydroxycarbamoyl-propyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-4-hydroxycarbamoyl-butyl)-benzoic acid;

3-(2-carboxy-4-hydroxycarbamoyl-butyl)-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoyl-pentyl)-benzoic acid;

3-(2-carboxy-3-hydroxycarbamoyl-propyl)-benzoic acid;

3-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid methyl ester;

3-(2-carboxy-3-hydroxyamino-propyl)-benzoic acid;

3-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid methyl ester;

3-(2-carboxy-5-hydroxycarbamoylmethylsulfanyl-pentyl)-benzoic acid;

3-(2-carboxy-6-hydroxycarbamoylmethyl-
sulfanylhexyl)-benzoic acid;

3-(2-carboxy-4-hydroxycarbamoylmethyl-sulfanylbutyl)-benzoic acid;

3-[2-carboxy-3-(3-hydroxycarbamoyl-propylsulfanyl)-propyl]-benzoic acid;

5 3-[2-carboxy-5-(4-hydroxycarbamoyl-butylsulfanyl)-pentyl]-benzoic acid;

3-{2-carboxy-5-[(hydroxy-methyl-carbamoyl)-methylsulfanyl]-pentyl}-benzoic acid;

10 3-tert-butyl-5-[2-carboxy-4-(1-hydroxycarbamoyl-propylsulfanyl)-butyl]-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-4-chloro-benzoic acid;

3-[2-carboxy-4-(1-hydroxycarbamoyl-propylsulfanyl)-butyl]-benzoic acid;

15 3-[2-carboxy-3-(1-hydroxycarbamoyl-propylsulfanyl)-propyl]-benzoic acid;

2-biphenyl-3-ylmethyl-5-hydroxycarbamoylmethyl-sulfanyl-pentanoic acid;

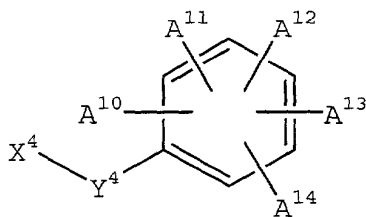
20 3'-(2-carboxy-5-hydroxycarbamoylmethylsulfanyl-pentyl)-biphenyl-3-carboxylic acid;

2-bromo-4-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-benzoic acid; and

enantiomers and pharmaceutically acceptable equivalents.

25

37. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XIV



XIV

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

5 X^4 is $-(CO)NHOH$ or $-N(OH)COH$;

Y^4 is a bond or a divalent linking group having from 1 to 9 carbon atom(s) and from 0 to 5 heteroatom(s) independently selected from the group consisting of oxygen, sulfur and nitrogen;

10 A^{10} , A^{11} , A^{12} , A^{13} and A^{14} are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, $-COOR^{43}$, $-COR^{43}$, $-NR^{43}R^{44}$, $-SR^{43}$, $-SOR^{43}$, $-SO_2R^{43}$, $-SO_2(OR^{43})$,
 15 $-(CO)NR^{43}R^{44}$, $-(CO)NR^{43}(CH_2)_nCOOH$, $-NR^{43}(CO)R^{44}$ or $-(CH_2)_nCOOH$, or any adjacent two of A^{10} , A^{11} , A^{12} and A^{13} form with the benzene ring a fused ring that is saturated or unsaturated, aromatic or non-aromatic, and carbocyclic or heterocyclic, said heterocyclic ring containing 1 or 2
 20 oxygen, nitrogen and/or sulfur heteroatom(s);

n is 1-3;

R^{43} and R^{44} are independently hydrogen, C_1 - C_9 alkyl, C_2 - C_9 alkenyl, C_2 - C_9 alkynyl, aryl, heteroaryl, carbocycle or

heterocycle; and

said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy, and fused ring are independently unsubstituted or substituted with one or more substituent(s).

38. The method of claim 37, wherein:

Y^4 is a bond or $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, $-O-$, $-S-$ or $-SO_2-$;

p and q are independently 0-4;

R^{45} , R^{46} , R^{47} , R^{48} , R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfinio, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s); and

A^{10} , A^{11} and A^{12} are each hydrogen.

39. The method of claim 37, wherein:

Y^4 is a bond;

A^{10} , A^{11} and A^{12} are each hydrogen;

A^{13} is hydroxy, phenoxy, benzyloxy, $-COOR^{43}$ or $-(CO)NHR^{44}$;

A¹⁴ is -COOR⁴³;

R⁴³ is hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl or C₂-C₄ alkynyl;

R⁴⁴ is benzyl; and

5 said benzyl, phenoxy and benzyloxy are independently unsubstituted or substituted with -COOR⁴³.

40. The method of claim 37, wherein:

Y⁴ is -(CR⁴⁵R⁴⁶)_p-W²-(CR⁴⁷R⁴⁸)_q-;

10 W² is -O- or -S-; R⁴⁵, R⁴⁶, R⁴⁷ and R⁴⁸ are each hydrogen;

A¹⁰, A¹¹ and A¹² are each hydrogen;

15 A¹³ is hydrogen, -COOH, phenyl or benzyloxy, wherein said phenyl and benzyloxy are independently unsubstituted or substituted with -COOR⁴³; and

A¹⁴ is -COOR⁴³.

41. The method of claim 37, wherein:

Y⁴ is a bond or -(CR⁴⁵R⁴⁶)_p-W²-(CR⁴⁷R⁴⁸)_q-;

20 W² is -CR⁴⁹R⁵⁰-, -NR⁴⁹-, -O-, -S- or -SO₂-;

p and q are independently 0-4;

25 R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹ and R⁵⁰ are independently hydrogen, C₁-C₉ alkyl, C₂-C₉ alkenyl, C₂-C₉ alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfinio, C₁-C₉ alkoxy, C₂-C₉ alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl,

carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s);

A¹⁰, A¹¹ and A¹² are each hydrogen;

5 A¹³ is hydrogen, nitro or C₁-C₄ alkoxy; and

A¹⁴ is hydroxy, phenoxy, benzyloxy, benzoyl or C₁-C₄ alkoxy, wherein said phenoxy, benzyloxy, benzoyl and alkoxy are independently unsubstituted or substituted with one or more substituent(s).

10

42. The method of claim 37, wherein the compound is selected from the group consisting of:

5-hydroxycarbamoyl-isophthalic acid monoethyl ester;

15 6-benzyloxy-N-hydroxy-isophthalamide acid methyl ester;

6,N-dihydroxy-isophthalamide acid;

6-benzyloxy-N-hydroxy-isophthalamide acid;

4-(3-hydroxycarbamoyl-propylsulfanylmethyl)-biphenyl-2,3'-dicarboxylic acid;

20 4-(4-hydroxycarbamoyl-butylsulfanylmethyl)-biphenyl-2,3'-dicarboxylic acid;

4-(2-hydroxycarbamoyl-ethylsulfanylmethyl)-biphenyl-2,3'-dicarboxylic acid;

25 3-(2-hydroxycarbamoyl-methylsulfanylethyl)-biphenyl-2,3'-dicarboxylic acid;

5-hydroxycarbamoylmethoxy-isophthalic acid;

3-hydroxycarbamoylmethoxy-benzoic acid;

3-(4-hydroxycarbamoyl-butoxy)-biphenyl-2,3'-
dicarboxylic acid;

3-(4-hydroxycarbamoyl-butoxy)-biphenyl-2,3'-
dicarboxylic acid;

5 3-(3-hydroxycarbamoyl-propoxy)-biphenyl-2,3'-
dicarboxylic acid;

3-(2-hydroxycarbamoyl-ethoxy)-biphenyl-2,3'-
dicarboxylic acid;

10 3-hydroxycarbamoylmethoxy-biphenyl-2,3'-dicarboxylic
acid;

3-hydroxycarbamoylmethoxy-biphenyl-2,3'-dicarboxylic
acid dimethyl ester;

2-hydroxycarbamoylmethoxy-benzoic acid;

2-hydroxycarbamoylmethoxy-benzoic acid methyl ester;

15 3-(2-hydroxycarbamoyl-ethoxy)-biphenyl-2,3'-
dicarboxylic acid dimethyl ester;

4-(4-cyano-benzyloxy)-N-hydroxy-benzamide;

3-[3-(2-hydroxycarbamoyl-ethyl)-phenoxymethyl]-
benzoic acid;

20 2,N-dihydroxy-benzamide;

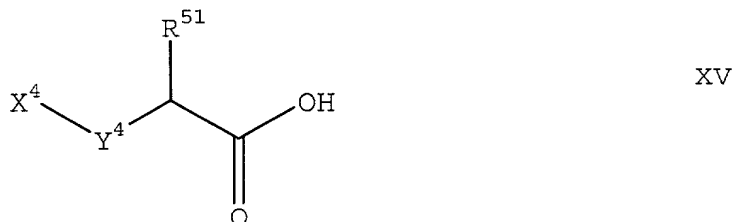
4-(4-fluoro-phenoxy)-N-hydroxy-3-nitro-benzamide;

N-hydroxy-2,5-bis-(2,2,2-trifluoro-ethoxy)-
benzamide;

N-hydroxy-2-(4-methyl-benzoyl)-benzamide; and

25 enantiomers and pharmaceutically acceptable
equivalents.

43. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XV



or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^4 is $-(\text{CO})\text{NHOH}$ or $-\text{N}(\text{OH})\text{COH}$;

Y^4 is a bond or a divalent linking group having from 1 to 9 carbon atom(s) and from 0 to 5 heteroatom(s) independently selected from the group consisting of oxygen, sulfur and nitrogen; and

R^{51} is hydrogen, $\text{C}_1\text{-C}_9$ alkyl, $\text{C}_2\text{-C}_9$ alkenyl, $\text{C}_2\text{-C}_9$ alkynyl, $\text{C}_1\text{-C}_9$ alkoxy or $\text{C}_2\text{-C}_9$ alkenoxy, wherein said alkyl, alkenyl, alkynyl, alkoxy and alkenoxy are independently unsubstituted or substituted with one or more substituent(s); provided that when Y is methylene, amine or oxygen, then R^{51} is not carboxyethyl.

44. The method of claim 43, wherein:

Y^4 is $-(\text{CR}^{45}\text{R}^{46})_p\text{-W}^2\text{-(CR}^{47}\text{R}^{48})_q\text{-}$;

W^2 is $-\text{CR}^{49}\text{R}^{50}\text{-}$, $-\text{NR}^{49}\text{-}$, $-\text{O-}$, $-\text{S-}$ or $-\text{SO}_2\text{-}$;

p and q are independently 0-4; and

R^{45} , R^{46} , R^{47} , R^{48} , R^{49} and R^{50} are independently hydrogen, $\text{C}_1\text{-C}_9$ alkyl, $\text{C}_2\text{-C}_9$ alkenyl, $\text{C}_2\text{-C}_9$ alkynyl, aryl,

49. A pharmaceutical composition comprising:

- (i) an effective amount of a NAALADase inhibitor for treating a retinal disorder or glaucoma; and
- (ii) a pharmaceutically acceptable carrier.